UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF INDIANA
INDIANAPOLIS DIVISION

ELI LILLY AND COMPANY, Plaintiff, v. TEVA PARENTERAL MEDICINES, INC., APP PHARMACEUTICALS, LLC, PLIVA HRVATSKA D.O.O., TEVA PHARMACEUTICALS USA INC., BARR LABORATORIES, INC., Defendants.	)	Case No. 1:10-cv-01376-TWP-DKL
ELI LILLY AND COMPANY 1:11-cv-00942-TWP-TAB, Consol Plaintiff, v. APP PHARMACEUTICALS, LLC 1:11-cv-00942-TWP-TAB, Consol Defendant v. FRESENIUS KABI USA, LLC 1:15-cv-00096-TWP-DKL Consol Defendant.	)	

FINDINGS OF FACT AND CONCLUSIONS OF LAW
FOLLOWING SECOND BENCH TRIAL HELD MAY 28, 2015

This is a Hatch-Waxman patent infringement action brought by Eli Lilly and Company ("Lilly"), the owner of U.S. Patent No. 7,772,209 (the "'209 patent"), against Defendants Teva Parenteral Medicines, Inc. ("Teva Parenteral"), Teva Pharmaceuticals USA, Inc. ("Teva

Pharmaceuticals") (collectively with Teva Parenteral, "Teva"), APP Pharmaceuticals, LLC ("APP"), Barr Laboratories, Inc. ("Barr"), and Pliva Hrvatska D.O.O. ("Pliva") (collectively, "Defendants") arising out of Defendants' filing of Abbreviated New Drug Applications ("ANDAs") with the FDA seeking approval to market the pemetrexed disodium products identified in Teva's ANDAs Nos. 90-352 and 90-674, APP's ANDA No. 90-384, and Barr's and Pliva's ANDA No. 91-111 (collectively, the "ANDA Products") and covered under the '209 patent. The '209 patent describes a method of administering a chemotherapy drug, pemetrexed disodium ("pemetrexed"), with vitamins, which is marketed by Lilly under the trade name ALITMA®.

This matter was before the Court for a second bench trial on May 28, 2015, on the issue of infringement of claims 9, 10, 12, 14, 15, 18, 19 and 21 (the "Asserted Claims") of the '209 patent". During the first trial, the parties jointly stipulated to induced infringement and proceeded to trial only on the issue of validity. As part of their stipulation, however, defendants reserved the right to litigate infringement if the Supreme Court granted the then-pending petition for writ of certiorari in *Lime-light Networks, Inc. v. Akamai Technologies, Inc*., 134 S. Ct. 2111 (2014) and reversed or vacated the Federal Circuits decision. Following the United States Supreme Court's decision in *Akamai*, the parties jointly moved to remand their pending appeal so that they could litigate the issue of infringement.

FINDINGS OF FACT

The Court has set forth the facts of this case in its ruling from the first bench trial on the issue of validity, including the history of the development of antifolate chemotherapy and specifically ALITMA®, and thus the facts are not repeated in detail here. (*See* Filing No. 336.)

The following constitutes the basic facts giving rise to this infringement action, and the relevant factual findings as it relates to the second bench trial on the issue of indirect infringement.

The patent-in-suit is U.S. Patent No. 7,772,209, which was issued to Lilly on August 10, 2010, and Lilly is the current owner of the '209 patent. The '209 patent covers the method of administration of ALIMTA®, requiring that physicians co-administer the drug with folic acid and vitamin B_{12} to reduce the incidence of patient toxicity caused by pemetrexed. Lilly sells pemetrexed in the United States under the trademark ALIMTA® for treatment of specific types of lung cancer and mesothelioma. The Defendants in this case seek FDA approval to market generic forms of pemetrexed, and further seek to sell their pemetrexed products with prescribing information (TX 3018) and patient information (TX 3017) that provides instructions to both doctors and patients that is identical to the methods described in the '209 patent.

Lilly is asserting claims 9, 10, 12, 15, 18, 19, and 21 of the '209 patent with respect to the ANDA Products. TX 1 at cols. 11-12. Each claim requires pretreatment with a specified amount of folic acid, up to 1000 μg, and with vitamin B_{12} in the amount of 55-1,500 μg in claims 12, 14 and 21, and 1000 μg in claims 15, 18, and 19, prior to administering pemetrexed. Claims 19, 21, and 22 further require a specific schedule for those pretreatments, and claims 15, 18 and 19 require administration of vitamin B_{12} by intramuscular injection. The Defendants' product labeling for their proposed generic versions of ALITMA® instructs doctors to follow exactly the claimed regimen, as the ANDA Products will be required to be distributed with materially identical labeling as that for ALITMA®. *See* 21 U.S.C. § 355(j)(2)(A)(v).

The primary focus of the infringement trial is on whether the steps of the claimed methods may be attributed to a single actor, thus supporting a finding that Defendants would induce infringement of the Asserted Claims. Specifically, the parties dispute whether physicians will

directly infringe the patent by directing or controlling the administration of folic acid to patients. Claim 12 of the '209 patent describes an improved method for administering pemetrexed disodium, comprising "a) administration of between 3500 µg and about 1000 µg of folic acid prior to the first administration of pemetrexed disodium; b) administration of about 500 µg to about 1500 µg of vitamin B12, prior to the first administration of pemetrexed disodium; and c) administration of pemetrexed disodium." TX. 1 at col. 11-12. The prescribing information for ALITMA® states that physicians administering the treatment should "instruct patients to initiate folic acid 400 mcg to 1000 mcg orally once daily beginning 7 days before the first dose of ALITMA®." TX 3018 at 2. The instructions also state that physicians should "[a]dminister vitamin B_{12} 1 mg intramuscularly 1 week prior to the first dose of ALITMA and every 3 cycles thereafter" and that physicians should "[a]dminister dexamethasone 4 mg by mouth twice daily the day before, the day of, and the day after ALITMA administration." *Id.* Both Lilly's and the Defendants' experts, Dr. Bruce A. Chabner, M.D. and Dr. Thomas K. Schulz, M.D., agreed that, following these labels, the doctor or other medical professional will administer the vitamin B_{12} by injection, and pemetrexed by infusion. Tr. 138, 139, 141, 189. However, it is the patient, at the instruction of the physician, who must obtain and take the folic acid.

I. CONCLUSIONS OF LAW

A. History of the Proceedings

In Hatch-Waxman actions, the issue of infringement is typically litigated before the generic companies have approval for their product and thus before they have sold any of the drug at issue. Generic manufacturers, such as Defendants, do not treat patients and therefore do not directly infringe; rather, Defendants may be held liable for infringement under 35 U.S.C. § 271(b) if they actively induce infringement of the '209 patent. As stated earlier, Defendants previously stipulated

that under the Court's claim construction (Filing No. 115) and under the then-current laws of infringement at the time of the first trial on August 19-29, 2013, the sale of its ANDA Products, in accordance with the proposed labeling for each of those respective ANDA Products, would infringe the Asserted Claims of the '209 patent, to the extent those claims were found valid and enforceable. The parties reserved the right to litigate the issue of infringement in the event that the Supreme Court granted the then-pending petition for writ of certiorari in *Akamai Techs. v. Limelight Networks, Inc.*, 692 F.3d 1301 (Fed. Cir. 2012) (*en banc*), and reversed or vacated the Federal Circuit's decision in *Akamai*.

On March 31, 2014, this Court issued a ruling finding that the Defendants had failed to show by clear and convincing evidence that the Asserted Claims of the '209 patent were invalid, finding in favor of Lilly that the Asserted Claims of the '209 patent are valid and enforceable. (Filing No. 336). Subsequent to the Court's ruling and issuance of final judgment, Defendants appealed this Court's ruling to the Federal Circuit. However, the parties jointly moved to remand the appeal in order to litigate the issue of infringement in light of the Supreme Court's decision in *Limelight Networks, Inc. v. Akamai Techs., Inc.*, 1134 S.Ct. 2111 (2014), in which the Supreme Court reversed the Federal Circuit's decision, and remanded the case to the Federal Circuit. The Supreme Court held that for direct infringement to occur—a requirement for finding inducement of infringement under § 271(b)—"performance of all of the claimed steps [must] be attributed to a single person." *Id.* at 2118.

Subsequent to the Supreme Court's ruling, the Federal Circuit issued a panel decision in *Akamai Techs., Inc. v. Limelight Networks, Inc.*, 786 F.3d 899 (Fed. Cir. 2015), in which it held there was no "divided infringement" under 35 U.S.C. § 271(a) where the patentee failed to demonstrate that the competitor's customers were acting as agents of or otherwise contractually

obligated to the competitor, or that the customers were acting in a joint enterprise when performing some steps of the patented method. *Akamai Technologies, Inc. v. Limelight Networks, Inc.*, 786 F.3d 899, 915 (Fed. Cir. 2015) *reh'g en banc granted, opinion vacated sub nom. Akamai Technologies, Inc. v. Limelight Networks, Inc.*, No. 2009-1372, 2015 WL 4759378 (Fed. Cir. Aug. 13, 2015) and *on reh'g en banc sub nom. Akamai Technologies, Inc. v. Limelight Networks, Inc.*, No. 2009-1372, 2015 WL 4760450 (Fed. Cir. Aug. 13, 2015). A petition for rehearing *en banc* was filed by the plaintiffs-appellants in *Akamai*, which was granted by the Federal Circuit court. *Akamai Technologies, Inc. v. Limelight Networks, Inc.*, No. 2009-1372, 2015 WL 4759378, at *1 (Fed. Cir. Aug. 13, 2015). The Federal Circuit, in an *en banc* per curiam opinion, unanimously set forth the law of divided infringement under 35 U.S.C. § 271(a) and vacated the *Akamai* panel decision. *Akamai Technologies, Inc. v. Limelight Networks, Inc.*, No. 2009-1372, 2015 WL 4760450 (Fed. Cir. Aug. 13, 2015) *(en banc*) (per curiam). The Federal Circuit also overruled its prior case law regarding divided infringement, "[t]o the extent [those] prior cases formed the predicate for the vacated panel decision," and no longer limited § 271(a) to principal-agent relationships, contractual arrangements, and joint enterprises, as the vacated panel decision held. *Id.* at *2, *4 n.3. Thus, for purposes of this case, the Court must apply this most current articulation of the law of divided infringement as stated by the Federal Circuit in its most recent ruling.

B. Current Articulation of the Law

Liability for inducement of infringement is predicated on a finding of direct infringement by a third party. *Limelight*, 134 S.Ct. at 2117. Under 35 U.S.C. § 271(a), direct patent infringement occurs where all steps of a claimed method are performed by or attributable to a single entity. *Akamai*, 2015 WL 4760450 at *1. "Where more than one actor is involved in practicing the steps, a court must determine whether the acts of one are attributable to the other

such that a single entity is responsible for the infringement." *Id.* On a claim for direct infringement of a method patent, the court will hold an entity responsible for others' performance of method steps under two circumstances: (1) where that entity directs or controls others' performance, and (2) where the actors form a joint enterprise. *Id.* With respect to the former requirement, the Federal Circuit concluded, in its *en banc* ruling, that "liability under § 271(a) can also be found when an alleged infringer conditions participation in an activity or receipt of a benefit upon performance of a step or steps of a patented method and establishes the manner or timing of that performance." *Id.* In those instances, the third party's actions are attributed to the alleged infringer "such that the alleged infringer becomes the single actor chargeable with direct infringement." *Id.* This determination is a question of fact to be made by this Court.

In *Akamai*, the plaintiff filed a patent infringement suit against the defendant, alleging infringement of a patent which claimed methods for delivering content over the Internet. The parties agreed that the defendant's customers—not the defendant itself—performed the "tagging" and "serving" steps in the claimed method of the patent-in-suit. At the trial court, the jury found that the defendant was responsible for its customers' activities, and was therefore liable for direct infringement. Relying upon the Federal Circuit's ruling in *Muniauction, Inc. v. Thomson Corp.*, 532 F.3d 1318 (Fed. Cir. 2008), the district court granted the defendant's motion for reconsideration, and held that as a matter of law there could be no liability. The Federal Circuit, in its recent *en banc* decision, reversed and reinstated the jury verdict, finding that the jury had substantial evidence from which it could find that the defendant directed or controlled its customers' performance of each remaining method step not performed by the defendant, such that all steps of the method were attributable to the defendant. *Akamai*, 2015 WL 4760450 at *3. Specifically, the Federal Circuit determined that there was substantial evidence demonstrating that

the defendant conditioned its customers' use of its content delivery network upon its customers' performance of the tagging and serving steps of the patent method, and that the defendant established the manner or timing of its customers' performance. *Id.* Because the customers were not merely taking the defendant's guidance and acting independently on their own, but rather had to perform the method steps in order to avail themselves of the defendant's service, the court found that the defendant was liable for direct infringement. *Id.* at *3-4.

Although the instant case involves the administration of a medical treatment, the factual circumstances are sufficiently analogous to those in *Akamai* to support a finding of direct infringement by physicians under § 271(a), and thus inducement of infringement by Defendants under § 271(b), under the legal standard recently set forth by the Federal Circuit. Defendants, relying upon now overruled case law on divided infringement, argue that the actions of the patient in taking folic acid prior to pemetrexed treatment cannot be attributed to the physician because the physician does not physically place the folic acid into the patients' mouth, and because patients are instructed to obtain folic acid, either by prescription or over the counter, and take it on their own. Although the parties present extensive arguments as to whether this constitutes the physician "administering" the folic acid, whether or not this satisfies the definition of "administer" is not relevant. What is relevant is whether the physician sufficiently directs or controls the acts of the patients in such a manner as to condition participation in an activity or receipt of a benefit—in this case, treatment with pemetrexed in the manner that reduces toxicities—upon the performance of a step of the patented method and establishes the manner and timing of the performance. Defendants argue that there is no way of knowing whether the patient will or will not actually take the folic acid, thus the physician lacks "control or direction" over this step of the patented process. However, as stated by the Supreme Court, "the patent is not infringed unless all the steps are

carried out" and "[e]ach element contained in a patent claim is deemed material to defining the scope of the patented invention." *Limelight*, 134 S. Ct. at 2117 (quoting *Warner–Jenkinson Co. v. Hilton Davis Chemical Co.,* 520 U.S. 17, 29 (1997)). Thus, the Court must assume that all steps of the Asserted Claims of the '209 patent will be carried out, and the only relevant question is whether the actions of the patient in taking folic acid as instructed may be attributable to the physician as a single actor.

One of the key steps set forth in the '209 patent is the administration of folic acid to the patient prior to the administration of pemetrexed. This is not merely a suggestion or recommendation, but a critical step in the patented method that has a specific purpose and direct impact on the outcome of the patented method. TX 1, at col. 11-12. The prescribing information requires physicians to "[i]nstruct patients to initiate folic acid 400 mcg to 1000 mcg orally once daily beginning 7 days before the first dose of ALITMA®." TX 3018 at 2. Additionally, the patient information states "**[i]t is very important to take folic acid . . . during your treatment with ALITMA to lower your chances of harmful side effects.** You must start taking 400-1000 micrograms of folic acid every day for at least 5 days out of the 7 days before your first dose of ALITMA." TX. 3017 at 2 (emphasis in original). It is clear from the patent, the prescribing information, and the patient information that taking folic acid in the manner specified is a condition of the patient's participation in pemetrexed treatment as described by the patent, and is necessary in order to receive the benefit of such treatment. If the patient fails to carry out this step, he or she would not receive the benefit of the patented method, i.e. a reduction of potentially life-threatening toxicities caused by pemetrexed. The physician, based upon the patented method, directs the manner and timing of the patient's ingestion of folic acid—400 to 1000 μg of folic acid for at least five days out of the seven days prior to and during pemetrexed administration—and the patient is

required to do so to receive the full benefit of the treatment. The Court cannot base a finding of non-infringement upon the mere possibility that some patients might not follow their physician's instructions and instead must look to the ANDA Products' labeling to determine, if all the patented steps are followed, whether it would infringe the Asserted Claims.

Lilly has shown, by a preponderance of the evidence that, in accordance with Defendants' proposed labeling, the physician directs or controls the patient's administration of folic acid such that the performance of all the claimed steps, including the administration of folic acid, can be attributed to a single person, i.e. the physician. The evidence showed that physicians specify both the "manner and timing" in detail, including prescribing an exact dose of folic acid and directing that it be ingested daily. Tr. 111–12. The Court finds that performance of all of the claimed steps of the '209 patent are attributed to the physician and would therefore constitute direct infringement under § 271(a); thus, the use the Defendants' ANDA Products would constitute inducement of infringement of the '209 patent by Defendants under § 271(b).

II. CONCLUSION

Based upon the foregoing findings of fact and conclusions of law, the Court concludes that Lilly has shown by a preponderance of the evidence that the Asserted Claims of the '209 patent would be infringed by the Defendants' ANDA Products based upon inducement of infringement by a single actor, the physician administering pemetrexed disodium in accordance with the claimed methods. Therefore, the Court finds that Defendants' ANDA Products indirectly infringe the Asserted Claims of the '209 patent, and finds in favor of Lilly and against Defendants. Final judgment shall issue separate from this Entry.

SO ORDERED.

Date: 8/25/2015

Tanya Walton Pratt

TANYA WALTON PRATT, JUDGE
United States District Court
Southern District of Indiana

DISTRIBUTION:

Anne N. DePrez
BARNES & THORNBURG LLP
adeprez@btlaw.com

Jan M. Carroll
BARNES & THORNBURG LLP
jan.carroll@btlaw.com

Terri L. Bruksch
BARNES & THORNBURG LLP
tbruksch@btlaw.com

James P. Leeds
ELI LILLY AND COMPANY
jleeds@lilly.com

Kandi Kilkelly Hidde
FROST BROWN TODD LLC
khidde@fbtlaw.com

Natasha E. Daughtrey
GOODWIN PROCTER LLP
ndaughtrey@goodwinprocter.com

Brian J. Prew
GOODWIN PROCTER, LLP
bprew@goodwinprocter.com

Daryl L. Wiesen
GOODWIN PROCTER, LLP
dwiesen@goodwinprocter.com

Elaine Herrmann Blais
GOODWIN PROCTER, LLP
eblais@goodwinprocter.com

Emily L. Rapalino
GOODWIN PROCTER, LLP
erapalino@goodwinprocter.com

Michael B. Cottler
GOODWIN PROCTER, LLP
mcottler@goodwinprocter.com

Adam L. Perlman
WILLIAMS & CONNOLLY LLP
aperlman@wc.com

Bruce Roger Genderson
WILLIAMS & CONNOLLY LLP
bgenderson@wc.com

Christopher T Berg
WILLIAMS & CONNOLLY LLP
cberg@wc.com

David M. Krinsky
WILLIAMS & CONNOLLY, LLP
dkrinsky@wc.com

Dov P. Grossman
WILLIAMS & CONNOLLY, LLP
dgrossman@wc.com

Ellen E. Oberwetter
WILLIAMS & CONNOLLY, LLP
eoberwetter@wc.com